

CLAIMS AMENDMENT

(Marked Up Version)

What is claimed is:

1. "twice amended"

A process for generating phosphorothioate substituted nucleic acids in vivo comprising:

- 1) preparing microbial culture media depleted of phosphate
- 2) adding thio-phosphate as an alternative source of phosphate to the media
- 3) culturing micro-organisms in the modified media containing thiophosphate such that thiophosphate enters into nucleotide precursor pools thereby enabling the synthesis of phosphorothioate internucleotide linkages.

2. The method of claim 1 used to generate phosphorothioate ds DNA, ss DNA, and/or RNA by the in vivo incorporation of thio-phosphate into nucleotide precursor pools.

3. "amended"

The method of claim 1 used to generate ds DNA, ss DNA, or RNA partially substituted with phosphorothioate linkages by the in vivo incorporation of a

mixture of thio-phosphate and phosphate into nucleotide precursor pools.

4. "amended"

The method of claim 1 wherein the cells cultured in thio-phosphate media or induced to uptake thio-phosphate are of eukaryotic origin.

(please substitute the following claim five for the pending claim five)

5. "twice amended"

The method of claim 1 where the alternative source of phosphate is a derivative of thiophosphate such as dithiophosphate or methylthiophosphate.